Medical Analysis Systems (formerly Navix, Inc.)

Rapid, Low-Cost DNA Diagnostic Technology

In 1995, DNA diagnostics required significant manpower, typically from the highly paid research-grade scientists, which made DNA diagnostic testing prohibitively expensive for clinical diagnostic facilities. Moreover, the capital equipment costs required to add DNA diagnostic capabilities to existing, protein-based laboratory diagnostic methods increased the already daunting capital burden. Navix, Inc., with its subcontractor Profile Diagnostics, Inc., submitted a proposal to the Advanced Technology Program's (ATP) 1995 focused program "Tools for DNA Diagnostics." They proposed to eliminate much of the complexity and to reduce the amount of new equipment needed by a clinical diagnostics laboratory. If successful, Navix could reduce the number of steps required for DNA diagnostics by containing all materials and reactions in a single reaction chamber. This reaction chamber could reduce the cost to administer each test from several hundred dollars to approximately $1 per test.

ATP awarded Navix cost-shared funds to pursue a focused research program. The company succeeded in creating a technique to identify disease-causing sequences of DNA from sample strands, and, in 1999, they received a patent for their efforts. However, this covered only part of the research and development plan. Business problems and technical failures prevented Navix from designing a system that could identify disease-causing strands in a single reaction chamber so that ordinary laboratory machines could process and interpret the results. After the close of the ATP-funded project in 1998, Navix merged with Medical Analysis Systems. A new market study showed that a competitor had entered the marketplace with a better DNA diagnostic product. Therefore, Medical Analysis Systems did not pursue further research into the technology. The company went out of business in 2003 due to business reasons unrelated to the ATP-funded project.

COMPOSITE PERFORMANCE SCORE
(based on a four star rating)
No Stars

Research and data for Status Report 95-08-0017 were collected during August - October 2003.

U.S. Market Share Threatened

In 1995, the U.S. in vitro diagnostic test manufacturers enjoyed a significant market share of the estimated $17 billion laboratory-use-only annual world market for DNA-based research. Trends throughout both the U.S. healthcare market and the global diagnostic market, however, showed the movement away from "for research only" products and toward more actual DNA-based in vitro diagnostic work. Moving from laboratory work to in vitro work required significantly lower capital and per-test costs. In addition, the global health problem of drug-resistant pathogens placed pressure on healthcare providers to be certain of the nature of the disease before they prescribed treatments. All of these factors put added pressure on the industry to transform DNA diagnostics from a prohibitively expensive research tool to an inexpensive diagnostic technique that could be made available to healthcare providers.

To assist that transition, ATP initiated a focused program in 1995 to fund innovations in "Tools for DNA Diagnostics." Navix, Inc. responded to that focused program with a proposal to create a DNA diagnostics tool that would attempt to eliminate sample preparation steps. The preparation steps represented the most expensive and time-consuming component of DNA diagnostic research.

New Method Could Reduce Costs and Meet Demand

Navix proposed to develop a single-step, homogenous, quantitative assay to detect specific DNA sequences using a process the company called Self-Detected Target-Cycling Reaction (SD-TCR). The proposed SD-TCR process would use a novel protein-assisted strand replacement reaction that incorporated into the assay a protein enzyme coupled to one strand of a DNA probe. This probe corresponded to the DNA sequence correlated with the disease of interest. When double-stranded DNA from a patient was introduced, the probe (covered with an enzyme that actively sought out target double-stranded DNA) would find and replace any areas in the patient's DNA that correlated with disease. This binding released the strand with the enzyme that, in turn, activated a second enzyme that would show as an amplified, colored diagnostic result. In short, if the color appeared, a mutation (or other sequence of interest) was present.

Factors put added pressure on the industry to transform DNA diagnostics from a prohibitively expensive research tool to an inexpensive diagnostic technique.

If successful, the SD-TCR process would dramatically reduce the number of required steps for typical DNA diagnostics to just one. Instead of the costly sample preparation steps, the Navix technology would not require any modification or manipulation of the sample DNA other than simple DNA isolation and its addition to the reaction chamber. After being added to the reaction chamber, the sample DNA would then be allowed to react at controlled temperatures for about an hour. If successful, the SD-TCR process would reduce the time required for DNA diagnostics from days to hours. Moreover, with the addition of a reaction chamber to the system, the cost of conducting a full test analysis would be dramatically reduced from hundreds of dollars per test to less than $1.

Navix Faces Technical Challenges

Navix's technical challenge was to coordinate the three distinct chemical reactions necessary for the SD-TCR technology into a single step. The reactions (DNA identification, amplification, and signal generation) were all possible when they occurred separately, but they needed to be integrated into a working system. Navix entered into a subcontractor agreement with Profile Diagnostics, Inc. to pursue integrating the three reactions. Both Navix and Profile Diagnostics had years of experience in optimizing stand-alone DNA identification, amplification, and signal generation reactions. Together, the team sought to create new DNA diagnostic protocols that would not require new automated instruments. Instead, they asked the question, What can an existing diagnostic laboratory accomplish, and how can we enable one-step DNA diagnostics with those materials?

Navix scientists believed that the materials in a DNA diagnostics laboratory could be integrated through two technically risky and complex steps. First, the scientists would have to compartmentalize and optimize the DNA identification and detection functions into different areas within the reaction chamber without risking contamination. Second, they would have to integrate the three different reactions so that each stage would be compatible with the others and there would be no possibility of premature signal color development that would lead to incorrect results. Navix proposed that they could tightly integrate these reactions in order to achieve a single-step, homogeneous DNA assay.

SD-TCR Process Could Bring DNA Diagnostic Testing into the Clinical Laboratory

Navix expected that its SD-TCR process would allow the rapid identification of those DNA sequences whose presence is correlated with the potential for genetic diseases, likelihood of future cancers, or other genetic sequences that do not cause disease, but might predispose individuals to illness. Navix scientists were aware that most of the costs for DNA diagnostics came from the use of separate equipment for identification, amplification, and signal generation. Therefore, the scientists proposed to conduct the reaction in one container.

The proposed reaction vessel would have all the necessary components to conduct the analysis so that, once sample double-stranded DNA was added to the reaction chamber, no further manual or automated additions or manipulations would be required. If any of the DNA sequences associated with disease were present, a cascade of chemical reactions would occur,

causing specific reactions that would lead to color-coded indicators that laboratory equipment could read and analyze. Moreover, they proposed a system that would be compatible with the clinical detection computer systems on the market in the mid-1990s so that diagnostic laboratories would not incur high costs to incorporate the Navix system into their diagnostics offerings.

Navix Seeks Funding for Concentrated, Focused Research

At the time of Navix's 1995 proposal, no other companies were working on projects similar to the SD-TCR chamber. ATP funding became necessary when Navix's internal corporate resources proved inadequate to fund such high-risk research. Without ATP's funding, the research would have taken significantly longer, because Navix and Profile Diagnostics would not have been able to devote eight scientists to concurrent, full-time research. ATP awarded Navix $1.97 million to conduct parallel, focused research with Profile Diagnostics over a two-year period.

Technical and Business Problems Forestall Success

Navix and Profile Diagnostics hoped their ATP-funded project would achieve the following milestones:

- A patent for a DNA amplification process within one year of ATP funding
- A patent for a DNA detection process within one year of ATP funding
- Clinical trials within 15 months of ATP funding
- FDA application submission within two years of ATP funding
- First sales within three years of ATP funding

Navix and Profile Diagnostics scientists succeeded in developing a two-stage reaction for DNA identification and amplification. During stage one, the target nucleic acid groups from the sample double-stranded DNA created bonds with probes in the reaction chamber containing nucleic acids indicative of disease. This released another series of molecules into the assay. During stage two of the reaction, specific sites within the reaction chamber bound with the molecules released from the first stage of the reaction. If future technology developed as expected, the enzyme on the released DNA strand would activate a second enzyme to catalyze a chemical reaction to convert a colorless substrate into a colored product that existing laboratory equipment could analyze. This technology led to Navix receiving a U.S. patent in 1999.

The SD-TCR process would dramatically reduce the number of required steps for typical DNA diagnostics to just one.

Technical problems with the stability of the processes within the reaction chamber as well as business issues delayed the project. By the end of the second year of the project, Navix had filed amplification and detection patents. The U.S. Patent and Trademark Office awarded the amplification patent. Navix then provided an additional $1 million in funds to continue the research. ATP extended the project by an additional five months to allow for further research.

At the end of February 1998, Navix's ATP-funded project concluded; however, the company had fallen short of their goals. Later in 1998, Navix merged with Medical Analysis Systems. After analyzing the market following the merger, Medical Analysis Systems decided against further research or efforts to commercialize the ATP-funded technology because other products had beaten Medical Analysis Systems to market.

By early 2003, Medical Analysis Systems closed due to business reasons unrelated to the ATP-funded project. The company could not remain solvent with the products it offered. The company earned no revenues from the ATP-funded project and commercialized no technology.

Conclusion

Navix and subcontractor Profile Diagnostics submitted a proposal to create a one-step DNA diagnostic reaction chamber that would reduce the per-test cost from several hundred dollars to less than $1. After achieving initial technical success, business and subsequent technical issues prevented Navix from reaching its ultimate goal of commercializing a one-step DNA diagnostic system. After a 1998 merger with Medical Analysis Systems, the company halted further research into its Self-Detected Target-Cycling Reaction process. Five years later, the company went out of business.

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PROJECT HIGHLIGHTS
Medical Analysis Systems (formerly Navix, Inc.)

Project Title: Rapid, Low-Cost DNA Diagnostic Technology (DNA Diagnostics Using Self-Detected Target-Cycling Reaction [SD-TCR])

Project: To develop a rapid, low-cost DNA diagnostic system that detects DNA sequences associated with disease and automatically triggers complementary cascade reactions for DNA amplification and signal generation using current clinical laboratory instruments.

Duration: 9/1/1995-2/28/1998
ATP Number: 95-08-0017

Funding (in thousands):

ATP Final Cost	$1,973	69%
Participant Final Cost	895	31%
Total	$2,868	

Accomplishments: Although no products resulted and the company did not completely meet their technical goals, Navix and subcontractor Profile Diagnostics pursued aggressive parallel research and created a two-step process to identify areas of DNA that correlate with disease. The effort led to two patent applications, one of which was granted in 1999:

- "Homogeneous diagnostic assay method utilizing simultaneous target and signal amplification" (No. 5,858,665: filed July 25, 1996, granted January 12, 1999)

Commercialization Status: Navix did not commercialize any products from its ATP-funded research. Business issues delayed research long enough for another competitor to beat Navix to the market. After Navix's merger with Medical Analysis Systems in 1998, the new company decided against pursuing further research or commercializing the reaction chamber product. The new company went out of business in 2003.

Outlook: Because Medical Analysis Systems failed, and other products on the market have surpassed the company's patented technology, the outlook for this technology is poor.

Composite Performance Score: No Stars

Number of Employees: 8 at project start; 0 as of September 2003 (the company has gone out of business).

Focused Program: Tools for DNA Diagnostics, 1995

Company:
Medical Analysis Systems (formerly Navix, Inc.)
(Medical Analysis Systems is no longer in business)

Contact: No available contact

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